Cyclic Quaternary Ammonium Salts. Part VII.[1] The Deoxygenation of Pyrido[1,2-*a*]pyrazinium 2-Oxide Salts

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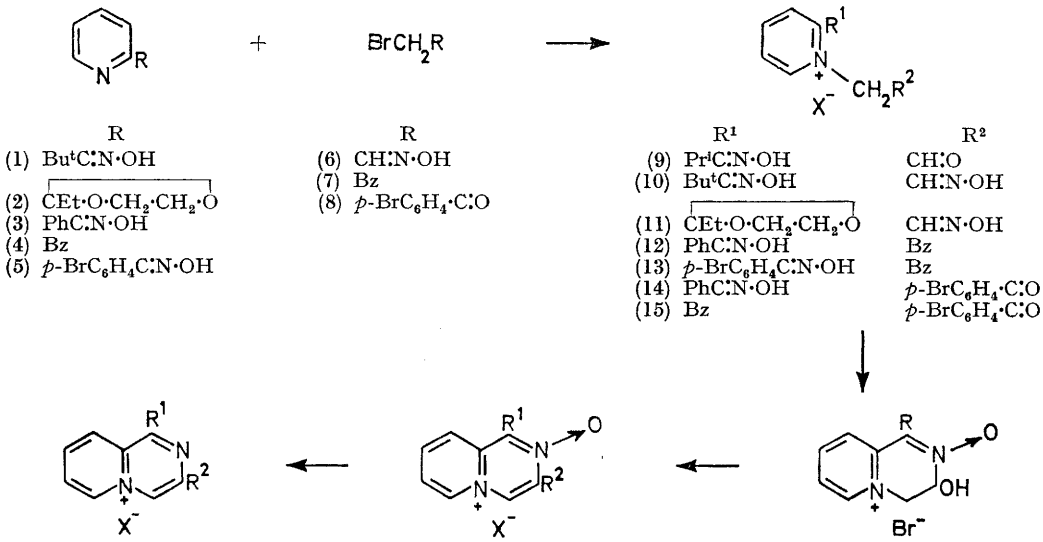
The relative ease of deoxygenation of 1-substituted, 3-substituted, and 1,3-disubstituted pyrido[1,2-*a*]pyrazinium 2-oxide salts has been investigated; large hydrocarbon substituents in the 1- or 3-position facilitate deoxygenation. Attempts to prepare 1,3-diphenylpyrido[1,2-*a*]pyrazinium 2-oxide salts from the quaternary salt formed between 2-benzoylpyridine oxime and phenacyl bromide gave, depending upon the reaction conditions, either the rearrangement product, 4-bromo-1,2-dihydro-1-oxo-2,3-diphenylpyrido[1,2-*a*]pyrazinium bromide, or 1,3-diphenylpyrido[1,2-*a*]pyrazinium bromide, the product of cyclisation accompanied by deoxygenation.

We have previously reported [2] the deoxygenation of the *N*-oxides (22) and (23) by boiling phosphorus tribromide, and have noted the resistance of the 1-methyl *N*-oxide (24) to such deoxygenation. Bradsher and Telang have reported [3] that the 3-methyl *N*-oxide (25) is unaffected by boiling phosphorus trichloride.

The required t-butyl, isopropyl, and ethyl 2-pyridyl ketones were prepared in yields of 66, 84, and 88%, respectively, by the action of the appropriate Grignard reagent on pyridine-2-carbonitrile.[4] In the case of the t-butyl compound, the triazine (36) was obtained as a by-product in 15% yield. The 2-pyridyl ketones



R	
(1)	$Bu^tC{:}N{\cdot}OH$
(2)	$CEt{\cdot}O{\cdot}CH_2{\cdot}CH_2{\cdot}O$
(3)	$PhC{:}N{\cdot}OH$
(4)	Bz
(5)	$p\text{-}BrC_6H_4C{:}N{\cdot}OH$

R	
(6)	$CH{:}N{\cdot}OH$
(7)	Bz
(8)	$p\text{-}BrC_6H_4{\cdot}C{:}O$

R^1	R^2
(9) $Pr^iC{:}N{\cdot}OH$	$CH{:}O$
(10) $Bu^tC{:}N{\cdot}OH$	$CH{:}N{\cdot}OH$
(11) $CEt{\cdot}O{\cdot}CH_2{\cdot}CH_2{\cdot}O$	$CH{:}N{\cdot}OH$
(12) $PhC{:}N{\cdot}OH$	Bz
(13) $p\text{-}BrC_6H_4C{:}N{\cdot}OH$	Bz
(14) $PhC{:}N{\cdot}OH$	$p\text{-}BrC_6H_4{\cdot}C{:}O$
(15) Bz	$p\text{-}BrC_6H_4{\cdot}C{:}O$

(16) R = Et

	R^1	R^2
(26)	Et	H
(27)	Pr^i	H
(28)	Bu^t	H
(29)	Ph	Ph
(30)	H	Ph
(31) *	H	H
(32) *	Ph	H
(33)	Me	H
(34)	H	Me
(35)	Ph	$p\text{-}BrC_6H_4$

	R^1	R^2
(17)	Et	H
(18)	Pr^i	H
(19)	Bu^t	H
(20)	Ph	Ph
(21) †	H	Ph
(22) *†	H	H
(23) *	Ph	H
(24) *	Me	H
(25) †	H	Me

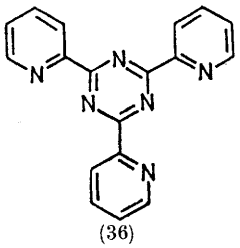
* Ref. 2. † Ref. 3.

In order to study the effect of 1- and 3-alkyl and -aryl substituents on the ease of deoxygenation of the title compounds and to investigate the resistance of the 1-methyl *N*-oxide (24) to deoxygenation, the *N*-oxides (17)—(25) were required. Of these, compounds (17)—(20) were previously unknown and their synthesis was therefore undertaken from the appropriate 2-pyridyl ketones.

were then converted into oximes (mixtures of geometrical isomers). By the procedure described by Huntress and Walter,[5] 2-benzoylpyridine oxime was separated into the *anti*-phenyl (37) and *syn*-phenyl (39) forms, the i.r. spectra (KBr discs) of which showed O–H stretching bands near 2840 and 3140 cm^{-1}, respectively, the

[1] Part VI, J. Adamson, E. C. Campbell, and E. E. Glover, *J. Chem. Soc.* (*C*), 1969, 2270.
[2] E. E. Glover and M. J. R. Loadman, *J. Chem. Soc.* (*C*), 1967, 2391.
[3] C. K. Bradsher and S. A. Telang, *J. Org. Chem.*, 1966, **31**, 941.
[4] H. R. Henze and M. B. Knowles, *J. Org. Chem.*, 1954, **19**, 1127.
[5] E. H. Huntress and H. C. Walter, *J. Amer. Chem. Soc.*, 1948, **70**, 3702.

hydrogen-bonded form (37) showing the expected shift to longer wavelength. Both forms gave the same quaternary salt (12) with phenacyl bromide.



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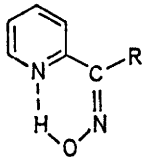
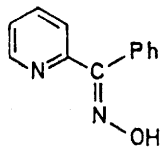


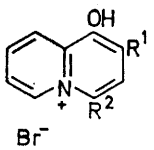
(37) R = Ph
(38) R = Pr^i



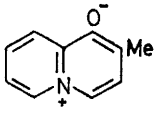
(39)

The oxime derived from isopropyl 2-pyridyl ketone was obtained as a gum from which crystals of the *anti*-isopropyl form (38) slowly crystallized; the configuration was assigned on the basis of the i.r. spectrum (KBr disc) which showed a bonded O–H stretching band near 2880 cm^{-1}. The gum was equally as satisfactory as the pure *anti*-isopropyl form (38) for conversion into the *N*-oxide (18).

The t-butyl *N*-oxide (19) was obtained by cyclising the quaternary salt (10) formed from 2-pyridyl t-butyl ketone oxime (1) and bromoacetaldehyde oxime (6),[6] with concentrated sulphuric acid, and the isopropyl *N*-oxide (18) was obtained by heating isopropyl 2-pyridyl ketone oxime and bromoacetaldehyde in a mixture of hydrobromic acid and acetonitrile. Treatment of the ethyl 2-pyridyl ketone oxime in acetonitrile with bromoacetaldehyde gave the hydroxy-dihydro-compound (16), which was subsequently dehydrated to the ethyl *N*-oxide (17) by boiling alcoholic hydrobromic acid. A previous attempt to prepare the ethyl *N*-oxide (17) by cyclising, with concentrated sulphuric acid, the quaternary salt (11), formed from the cyclic acetal (2) and bromoacetaldehyde oxime failed, the product of the reaction being 1-hydroxy-2-methylquinolizinium bromide (40).



	R^1	R^2
(40)	Me	H
(41)	H	H
(42)	Me	Br

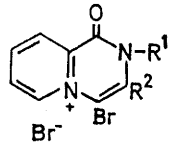


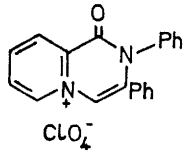
(43)

The hydroxy-compound (40) gave a blue colour with neutral iron(III) chloride solution, and its u.v. spectrum (water) showed good agreement with that reported[7] for 1-hydroxyquinolizinium bromide (41). The u.v. spectra of the hydroxy-compound (40) in 2N-hydrobromic acid, in aqueous 2N-sodium hydroxide, and in water showed that in water the phenolic form (40) is in equilibrium with the betaine (43). Like the parent hydroxy-compound (41),[7] the methyl derivative (40) was readily brominated; the product was assumed, for obvious mechanistic reasons, to be the 4-bromo-compound (42).

Attempts to form the 1,3-diphenyl *N*-oxide (20) by cyclising, with concentrated sulphuric acid, the quaternary salt (12) formed from 2-benzoylpyridine oxime and phenacyl bromide failed; the product was the bromolactam (44) formed by a reaction in which a Beckmann rearrangement had preceded cyclisation and subsequent bromination. The involvement of a Beckmann rearrangement was demonstrated by the formation of the lactam (47) directly when 2-picolinanilide was heated in acetonitrile with phenacyl bromide and the product converted into the perchlorate salt. That bromination had occurred, probably as the final stage of the reaction and as a result of the oxidation of the bromide ion to bromine by the sulphuric acid, was demonstrated by cyclising the perchlorate salt of (12) in sulphuric acid; the unbrominated lactam (47) was obtained which could be subsequently brominated, giving the bromolactam (44). The location of the bromine atom in the

	R^1	R^2
(44)	Ph	Ph
(45)	*p*-BrC$_6$H$_4$	Ph
(46)	Ph	*p*-BrC$_6$H$_4$





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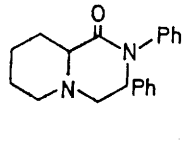

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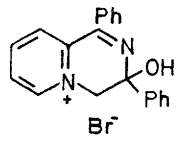


(49)

4-position of the lactam ring of (44) was shown by comparing the u.v. spectra of aqueous solutions of the brominated and unbrominated lactams (44) and (47). The former showed a bathochromic shift of 11 nm of the longest wavelength maximum, which would not be expected if the bromine atom had entered the *para*-position of either of the phenyl groups. Further, indirect evidence for the position of bromination was obtained by cyclising, with concentrated sulphuric acid, the quaternary salt (13) from *p*-bromophenyl 2-pyridyl ketone oxime and phenacyl bromide, giving the dibromo-lactam (45). Similarly, cyclisation of the quaternary salt (14) from 2-benzoylpyridine oxime and *p*-bromophenacyl bromide gave the corresponding dibromo-lactam (46). Hydrogenation and basification of both the unbrominated lactam (47) and the bromolactam (44) gave the base (48).

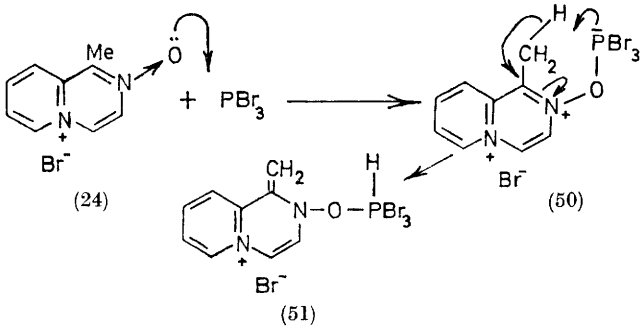
Cyclisation of the phenacyl quaternary salt (12) in boiling 48% hydrobromic acid gave the 1,3-diphenyl aromatic bromide (29) *via* the intermediate hydroxy-compound (49); cyclisation was accompanied by deoxygenation of the oxime nitrogen atom. The structure (29) was established by preparing the known bromo-derivative (35)[8] by similarly cyclising the quaternary

[6] D. H. Corr and E. E. Glover, *J. Chem. Soc.*, 1965, 5816.
[7] A. Fozard and G. Jones, *J. Chem. Soc.*, 1963, 2203.
[8] F. Kröhnke, H. Schnegelberger, and W. Weis, *Chem. Ber.*, 1964, **97**, 3566.

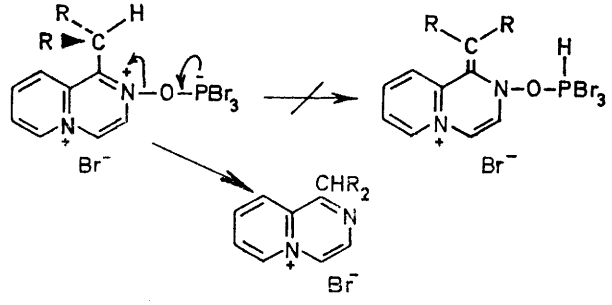
salt (14) formed from 2-benzoylpyridine oxime and *p*-bromophenacyl bromide.

The *N*-oxides (17)—(19) and (21)—(25) were deoxygenated as shown in Table 3. The heterogeneous nature of the deoxygenation reaction and the moderate yields obtained in some cases made a quantitative estimation of the ease of deoxygenation difficult. However, a study of the reaction temperature giving maximum yields indicated that large substituents in the 1- or 3-position facilitated deoxygenation. Thus the *N*-oxides having large 1-alkyl substituents were best deoxygenated in boiling phosphorus trichloride; use of the higher-boiling phosphorus tribromide gave rise to a violent reaction and extensive decomposition. The cyclisation of the quaternary salt (12) in hydrobromic acid to give the 1,3-diphenyl compound (29) instead of the expected *N*-oxide (20) provides supporting evidence for the steric influence of large 1- and 3-substituents on the ease of deoxygenation.

A possible explanation of the previously reported [2] resistance of the 1-methyl *N*-oxide (24) to deoxygenation is its conversion in phosphorus tribromide to the presumably more stable tautomer (51) *via* the transition state (50). Such stabilisation of the 1-methyl *N*-oxide



might be expected either to inhibit the deoxygenation reaction or at least to raise its activation energy. The latter was found to be the case, since deoxygenation was eventually accomplished by heating the *N*-oxide with phosphorus tribromide in a sealed tube at 190°. The relative ease of deoxygenation of the other 1-alkyl *N*-oxides (17)—(19) provides supporting evidence for this explanation; such compounds cannot tautomerise after reaction with phosphorus tribromide since steric interaction between the 1-alkyl substituent and the *peri*-hydrogen atom prevents the α-carbon atom of the alkyl substituent becoming sp^2 hybridised. Deoxygenation, therefore, readily follows reaction between the *N*-oxide function and phosphorus tribromide.



Additional evidence is found in the smooth deoxygenation in boiling phosphorus tribromide of the 3-methyl *N*-oxide (25), previously reported by Bradsher and Telang [3] to be unaffected by boiling phosphorus trichloride. The conversion of the 3-methyl *N*-oxide, after reaction with phosphorus tribromide, into a more stable tautomeric form is not mechanistically feasible.

EXPERIMENTAL

M.p.s were determined with a Kofler hot-stage apparatus; u.v. spectra were obtained with a Perkin-Elmer 137 spectrometer.

2-Pyridyl t-Butyl Ketone and Tri-(2-pyridyl)-s-triazine (36).—The Grignard reagent prepared under nitrogen from magnesium (9·5 g) and t-butyl bromide (51·5 g) in ether (175 ml) was stirred for 16 h at room temperature. After the addition of ether (350 ml) the solution was filtered and rapidly added to a stirred solution of pyridine-2-carbonitrile (15·6 g) in ether (240 ml), and the resulting solution was stirred for 16 h at room temperature. Ice-cold 4N-hydrochloric acid was then added and the aqueous layer was separated. The ether layer was further washed with four portions (25 ml) of 4N-hydrochloric acid and the combined acid layers were basified with ammonia. The precipitated solid gave the triazine [9] (2·31 g, 15%) as needles, m.p. 253—254° (from aqueous methanol) (Found: C, 69·4; H, 4·0; N, 26·8. Calc. for $C_{18}H_{12}N_6$: C, 69·2; H, 3·9; N, 26·9%) (lit.,[9] m.p. 244—245°. A sample prepared by the procedure of ref. 9 but with lithium hydride instead of sodium hydride had m.p. 246—248°. The i.r. and u.v. spectra of the two samples were identical and a mixture of the two samples had m.p. 247—250°). The filtrate was extracted with ether (5 × 50 ml) and the dried extract was distilled, giving the ketone (16·1 g, 66%), b.p. 103—104° at 20 mmHg (lit.,[4] yield 46%, b.p. 108—110° at 25 mmHg) (Found: C, 74·0; H, 7·9; N, 9·2. Calc. for $C_{10}H_{13}NO$: C, 73·6; H, 8·0; N, 8·6%). The oxime (69% yield) gave needles, m.p. 123—124° (from aqueous ethanol) (lit.,[10] 118—119°) (Found: C, 67·7; H, 7·9; N, 15·55. Calc. for $C_{10}H_{14}N_2O$: C, 67·4; H, 7·9; N, 15·7%).

Isopropyl 2-Pyridyl Ketone Oxime.—A solution of isopropyl 2-pyridyl ketone [10] (4 g), prepared (84%) as described for the t-butyl ketone, in ethanol (10 ml) and water (2 ml) was treated with hydroxylamine hydrochloride (3 g) and sodium hydroxide (5·6 g). The mixture was boiled under reflux for 10 min, cooled, neutralised with 4N-hydrochloric acid (phenolphthalein as external indicator), and extracted with ether. Evaporation of the dried extract gave a gum (3·6 g, 82%) from which crystals separated during 3—4 weeks. Recrystallisation from light petroleum (b.p. 60—80°) gave the anti-*isopropyl oxime* as needles, m.p. 87—88° (Found: C, 65·45; H, 7·1; N, 16·7. $C_9H_{12}N_2O$ requires C, 65·8; H, 7·4; N, 17·1%). Bertucat [10] reported an oxime, presumably a mixture of geometrical isomers, m.p. 38—40°.

2-(2-Ethyl-1,3-dioxolan-2-yl)pyridine (2).—This was prepared (65%) from ethyl 2-pyridyl ketone [obtained (88%)

[9] E. O. Leonard, C. G. Skinner, E. M. Lansford, and W. Shive, *J. Amer. Chem. Soc.*, 1959, **81**, 907.
[10] S. Bertucat, *Compt. rend.*, 1951, **232**, 1758.

as described for the t-butyl ketone] by the procedure described [11] for the methyl analogue. The *base* had b.p. 89° at 0·6 mmHg (Found: C, 67·05; H, 7·3; N, 7·9. $C_{10}H_{13}NO_2$ requires C, 67·0; H, 7·3; N, 7·8%).

1-*Hydroxy*-2-*methylquinolizinium Bromide* (40).—A solution of the quaternary salt (11) (0·83 g) in 48% hydrobromic acid (10 ml) was boiled under reflux for 30 min and then evaporated to dryness under reduced pressure. The residue was triturated with ethanol–ether and the resulting solid was recrystallised from chloroform–ethanol–methylene chloride giving the *bromide hemihydrate* as a pale yellow amorphous solid, m.p. 167—169° (0·53 g, 81%) (Found: C, 48·2; H, 4·4; N, 5·5. $C_{10}H_{10}BrNO$, $0·5H_2O$ requires C, 48·2; H, 4·45; N, 5·6%). The *picrate* gave yellow needles, m.p. 156—158° (from water) (Found: C, 49·6; H, 3·2; N, 14·2. $C_{16}H_{12}N_4O_8$ requires C, 49·5; H, 3·1; N, 14·4%).

4-*Bromo*-1-*hydroxy*-2-*methylquinolizinium Bromide* (42).—A solution of the hydroxy-bromide (40) (0·2 g) in a mixture of bromine (1 ml) and 48% hydrobromic acid (2·5 ml) was set aside at room temperature for 30 min, then heated (100°) for 1 h. Addition of acetone to the cooled solution precipitated the *bromide*, which gave buff needles, m.p. 209—211° (decomp.) (from acetone–48% hydrobromic acid) (0·18 g, 70%) (Found: C, 37·8; H, 3·0; N, 4·2. $C_{10}H_9Br_2NO$ requires C, 37·65; H, 2·8; N, 4·4%).

1-*Ethyl*-3-*hydroxy*-3,4-*dihydropyrido*[1,2-a]*pyrazinium Bromide* 2-*Oxide* (16).—A solution of ethyl 2-pyridyl ketone oxime [12] (1·0 g) and bromoacetaldehyde (1·0 g) in acetonitrile (2 ml) was boiled under reflux for 1·5 h. Addition of ether (50 ml) precipitated a gum which was triturated with ether followed by ethanol–acetone. The resulting solid gave the *bromide* as buff prisms, m.p. 153—155° (decomp.) (from ethanol–di-isopropyl ether) (0·88 g, 48%) (Found: C, 43·8; H, 4·8; N, 10·1. $C_{10}H_{13}BrN_2O_2$ requires C, 44·0; H, 4·8; N, 10·3%). The *picrate* yielded pale yellow plates, m.p. 172—174° (decomp.) (from water) (Found: C, 45·6; H, 3·6; N, 16·7. $C_{16}H_{15}N_5O_9$ requires C, 45·6; H, 3·6; N, 16·6%).

p-*Bromophenyl* 2-*Pyridyl Ketone*.—The Grignard reagent from *p*-dibromobenzene (26·2 g) and magnesium (3·26 g) in ether (70 ml) was stirred for 5 h under nitrogen. It was then filtered and added rapidly to a stirred solution of pyridine-2-carbonitrile (10·4 g) in ether (40 ml) under nitrogen. The solution was stirred for 16 h and then hydrolysed with ice-cold 4N-hydrochloric acid (75 ml). The ethereal layer was separated and washed with 4N-hydrochloric acid (4 × 25 ml). The combined acid layers were then basified with sodium carbonate and the separating ketone was extracted into ether. The dried extract was evaporated and the residue was distilled, giving the ketone, b.p. 164—168° at 0·7 mmHg (lit.,[13] 140—150° at 0·2 mmHg). The analytical sample, obtained by sublimation of the solidified distillate, had m.p. 37—40° (16·9 g, 64%) (Found: C, 55·4; H, 3·2; N, 4·8. $C_{12}H_8BrNO$ requires C, 55·0; H, 3·1; N, 5·3%). The *oxime* (80% yield) gave needles, m.p. 150—152° (from aqueous ethanol) (Found: C, 51·75; H, 3·1; N, 10·2. $C_{12}H_9BrN_2O$ requires C, 52·0; H, 3·3; N, 10·1%).

3,4-*Dihydro*-3-*hydroxy*-1,3-*diphenylpyrido*[1,2-a]*pyrazinium Bromide* (49).—A solution of the bromide (12) (0·55 g) in 48% hydrobromic acid (5 ml) was boiled under reflux for 10 min and then evaporated to dryness under reduced pressure. The residual gum was triturated with ether and then ethanol–acetone until it solidified. The bromide (0·34 g, 64%) crystallised from ethanol–di-isopropyl ether as an amorphous solid, m.p. 256—259° (decomp.) (Found: C, 62·95; H, 4·35; N, 7·4. $C_{20}H_{17}BrN_2O$ requires C, 63·0; H, 4·5; N, 7·35%).

1,3-*Diphenylpyrido*[1,2-a]*pyrazinium Bromide* (29).—A solution of the bromide (12) (0·7 g) in 48% hydrobromic acid (7 ml) was boiled under reflux for 6 h, then evaporated to dryness, and the residue was triturated with ethanol–ether until it solidified. The *bromide* gave pale yellow needles of the monohydrate, m.p. 266—268° (decomp.) (from ethanol) (0·36 g, 54%) (Found: C, 62·75; H, 4·8; N, 7·6. $C_{20}H_{15}BrN_2,H_2O$ requires C, 63·0; H, 4·5; N, 7·35%). The bromide could also be obtained by boiling the intermediate hydroxy-compound (49) in 48% hydrobromic acid. The *perchlorate* gave pale yellow needles, m.p. 264—265° (from methanol) (Found: C, 62·8; H, 3·95; N, 6·9. $C_{20}H_{15}ClN_2O_4$ requires C, 62·75; H, 3·95; N, 7·3%). The *picrate* gave yellow needles, m.p. 237—238° (decomp.) (from aqueous methanol) (Found: C, 61·2; H, 3·5; N, 13·7. $C_{26}H_{17}N_3O_7$ requires C, 61·1; H, 3·35; N, 13·7%).

3-(p-*Bromophenyl*)-1-*phenylpyrido*[1,2-a]*pyrazinium Bromide* (35).—This was prepared (67%) from the bromide (14) by the procedure described for compound (29). The bromide gave yellow prisms of the monohydrate, m.p. 363—366° (decomp.) (from aqueous ethanol) (lit.,[8] m.p. 355—357°) (Found: C, 52·4; H, 3·6; N, 6·4. Calc. for $C_{20}H_{14}Br_2N_2,H_2O$: C, 52·2; H, 3·5; N, 6·1%). The sample was identical with that [m.p. 363—366° (decomp.)] obtained by the procedure of ref. 8.

4-*Bromo*-1,2-*Dihydro*-1-*oxo*-2,3-*diphenylpyrido*[1,2-a]-*pyrazinium Bromide* (44).—A solution of the bromide (12) (1·2 g) in concentrated sulphuric acid (3 ml) was heated on a boiling-water bath for 10 min. Ether was added to the cooled solution and the precipitated gum was separated and washed with more ether. The gum was then dissolved in 48% hydrobromic acid (1 ml) and the *bromide* was precipitated with ethanol–ether. It yielded yellow plates (from methanol) which slowly decomposed without melting below 330° (0·68 g, 98%; based on available bromine) (Found: C, 52·7; H, 3·2; N, 6·1. $C_{20}H_{14}Br_2N_2O_5$ requires C, 52·4; H, 3·1; N, 6·1%). The *perchlorate* gave yellow needles, m.p. 317—320° (decomp.) (from aqueous methanol) (Found: C, 50·3; H, 3·2; N, 6·3. $C_{20}H_{14}BrClN_2O$ requires C, 50·3; H, 2·95; N, 5·9%). The perchlorate could also be obtained by cyclising the perchlorate salt (12; X = ClO_4) with concentrated sulphuric acid and adding bromine during the reaction.

1,2-*Dihydro*-1-*oxo*-2,3-*diphenylpyrido*[1,2-a]*pyrazinium Perchlorate* (47).—(i) A solution of the perchlorate (12; X = ClO_4) (0·45 g) in concentrated sulphuric acid (2 ml) was heated on a boiling-water bath for 10 min. Ether was added to the cooled solution and the precipitated gum was dissolved in 60% perchloric acid (1·0 ml). The *perchlorate* was precipitated with ethanol–ether and yielded yellow needles, m.p. 273—275° (from aqueous methanol) (0·39 g, 91%) (Found: C, 60·2; H, 3·75; N, 7·5. $C_{20}H_{15}ClN_2O_5$ requires C, 60·2; H, 3·8; N, 7·0%).

(ii) A solution of 2-picolinanilide (0·5 g) and phenacyl

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TABLE 1

Quaternary salts of 2-substituted pyridines

	Precursors			Heating		Product		Cryst.	Yield		Found (%)			Reqd. (%)		
	Wt./g		Wt./g Solvent	Time/h	Temp.		X	solvent	(%)	M.p.	C	H	N	C	H	N
(1)	0·5	(6)	0·4 None [a]	0·5	100°	(10)	Br [b]	EtOH–EtOAc	81	207—210°						
						(10)	$C_6H_2N_3O_7$	H_2O		185—187	46·5	4·4	18·1	46·6	4·3	18·1
(2)	1·0	(6)	0·85 None [c]	168	20	(11)	Br	EtOH–Pr^i_2O	51	178—180 [d]	45·4	5·3	8·9	45·4	5·4	8·8
(3)	1·0	(7)	1·0 MeCN(2 ml)	2·5	Reflux	(12)	Br [e]	$MeNO_2$	45	205—207 [d]	60·2	4·1	7·2	60·5	4·3	7·05
						(12)	ClO_4	EtOH–Pr^i_2O		194—196	57·6	4·1	6·9	57·6	4·1	6·7
(5)	1·0	(7)	0·72 MeCN(2 ml)	3	Reflux	(13)	Br [e]	$MeNO_2$–Pr^i_2O	50	194—197 [d]	50·3	3·3	5·9	50·4	3·4	5·9
(3)	1·0	(8)	1·4 MeCN(3 ml)	2	Reflux	(14)	Br [e]	$MeNO_2$	40	202—204	50·6	3·4	5·8	50·4	3·4	5·9
(4)	1·83	(8)	2·79 MeCN(7·5 ml)	1	Reflux	(15)	Br [f]	EtOH–Pr^i_2O	30 [e]	187—188	52·5	3·35	3·2	52·1	3·3	3·0

[a] After reaction the gum was triturated with ether until solid. [b] Satisfactory analyses could not be obtained. [c] After reaction the gum was dissolved in n-propanol (1 ml), di-isopropyl ether was added to initiate precipitation, and the solution was set aside for a further day. [d] Decomp. [e] After reaction the solution was treated with ether and the precipitated gum was triturated with ether until solid. [f] Lit.,[8] yield 50%, m.p. 259—261°.

TABLE 2

2-Oxides of pyrido[1,2-*a*]pyrazinium salts

	Precursor			Heating			Product		Cryst.	Yield		Found (%)			Reqd. (%)		
	Wt./g	X	Reagent(s)	Time/min	Temp.		X		solvent	(%)	M.p.	C	H	N	C	H	N
(16)	0·7	Br	48%HBr(0·5 ml)–EtOH (4 ml)	15	Reflux	(17) [a]	Br		EtOH–Pr^i_2O	71	191—194 [b]	45·9	4·2	11·1 [c]	45·5	4·6	10·6 [c]
						(17)	ClO_4		MeOH–EtOH		184—186	44·1	4·2	10·2	43·7	4·0	10·2
(9) [d]			48%HBr(0·2 ml)–MeCN (2 ml)	180	Reflux	(18) [a]	Br		EtOH–Pr^i_2O	21	162—164	46·2	5·4	9·55 [c]	46·0	5·3	9·75 [c]
						(18)	$C_6H_2N_3O_7$	H_2O			199—201 [b]	49·4	4·05	17·4	48·9	3·6	16·8
(10)	0·7	Br	Conc. H_2SO_4 (3 ml)	5	100°	(19)	Br		EtOH–Pr^i_2O	48	193—196 [b]			10·1			9·9
						(19)	ClO_4		EtOH		176—179 [b]	47·7	5·2	9·7	47·6	5·0	9·25
						(19)	$C_6H_2N_3O_7$	H_2O			168—170	49·9	4·0	15·8	50·1	4·0	16·2

[a] Ether was added and the precipitated gum was triturated with EtOH–Me_2CO until solid. [b] Decomp. [c] For hemihydrate. [d] Prepared *in situ* from isopropyl 2-pyridyl ketone oxime (1·0 g) and bromoacetaldehyde (0·8 g). [e] For monohydrate.

TABLE 3

Deoxygenation of pyrido[1,2-*a*]pyrazinium 2-oxide salts

Starting *N*-oxide (X = Br)	Reagent	Heating time/min	Product	X	Cryst. solvent	Yield (%)	M.p.	Found (%) C	H	N	Required (%) C	H	N
(17)	PBr_3	10(120°)	(26) [a]	PF_6	MeOH–Pr^i_2O	50	181—184° [b]	39·6	3·5	9·6	39·5	3·65	9·2
(18)	PCl_3	5(reflux)	(27) [c]	ClO_4	EtOH–Pr^i_2O	83	138—140	48·0	4·6	10·3	48·45	4·8	10·3
(19)	PCl_3	5(reflux)	(28) [c]	ClO_4	EtOH–Pr^i_2O	69	172—175	50·1	5·4	10·4	50·3	5·3	9·8
			(28)	$C_6H_2N_3O_7$	H_2O		161—162	51·9	4·1	17·1	52·05	4·1	16·9
(21) [d]	PBr_3	20(reflux)	(30)	Br	EtOH–Pr^i_2O	67	298—300 [b]	58·8	3·8	9·4	58·5	3·9	9·8
(22) [d,e]	PBr_3	20(reflux)	(31) [e]	Br		58							
(23) [e]	PBr_3	20(reflux)	(32) [e]	Br		54							
(24) [e]	PBr_3	25(190°) [f]	(33) [e]	ClO_4	MeOH–EtOH	67	192—194 [b]	44·3	3·75	11·45	44·2	3·7	11·45
			(33)	$C_6H_2N_3O_7$	EtOH–H_2O		174—175 [b]	48·3	3·15	18·5	48·3	3·0	18·75
(25) [d]	PBr_3	25(reflux)	(34)	Br	MeOH–Pr^i_2O	71	>330 [g]	47·6	4·0	12·0	48·0	4·0	12·45
			(34)	$C_6H_2N_3O_7$	H_2O		173—174	47·9	2·8	18·8	48·3	3·0	18·75

[a] The crude product was dissolved in ethanol and treated with 60% hexafluorophosphoric acid followed by ether. [b] Decomp. [c] The crude product was washed with ether, dissolved in ethanol, and treated with 60% perchloric acid followed by ether. [d] Ref. 3. [e] Ref. 2. [f] Heated in a sealed tube. [g] Slowly decomposed without melting.

TABLE 4

U.v. spectra *

Compound	X	$\lambda_{max.}$/nm	log ε
(17)	ClO_4	194, 224, 265, 318, 349sh, 363	4·09, 4·21, 3·86, 3·73, 3·78, 3·81
(18)	Br	196, 226, 257sh, 272, 305sh, 321, 335, 363	4·1, 4·11, 3·73, 3·65, 3·61, 3·67, 3·66, 3·52
(19)	ClO_4	194, 226, 238, 247, 255, 275sh, 337, 361sh	4·14, 3·98, 3·99, 4·02, 3·98, 3·52, 3·8, 3·67
(21)	Br	200, 224, 259, 280, 360	4·49, 4·24, 4·19, 4·16, 3·92
(26)	PF_6	199sh, 211, 235, 280, 292, 305sh, 321, 334	4·17, 4·2, 4·31, 3·53, 3·56, 3·67, 3·93, 3·94
(27)	ClO_4	198sh, 211, 235, 278, 291, 307sh, 322, 335	4·12, 4·15, 4·27, 3·51, 3·55, 3·67, 3·88, 3·91
(28)	ClO_4	210, 236, 248sh, 256, 283sh, 321, 334	4·06, 4·13, 3·89, 3·84, 3·36, 3·84, 3·9
(29)	ClO_4	196, 229sh, 265, 365	4·68, 4·3, 4·26, 3·95
(30)	Br	203, 225, 254, 307, 353	4·47, 4·35, 4·24, 4·06, 4·08
(33)	ClO_4	209, 234, 278, 292, 306sh, 320, 334	4·16, 4·27, 3·47, 3·53, 3·69, 3·93, 3·96
(34)	Br	202, 211sh, 235, 257sh, 276, 290, 328, 341	4·31, 4·28, 4·21, 3·49, 3·49, 3·44, 3·87, 3·91
(35)	Br	198, 231, 275, 320, 363	4·64, 4·38, 4·32, 4·15, 4·13
(36) †		248, 284	4·42, 4·58
(40)	Br	208, 234, 345, 380sh	4·48, 4·11, 3·99, 3·55
(40) [a] ‡	Br	250sh, 270sh, 380	3·85, 3·58, 3·93
(40) [a] §	Br	343	4·10
(42)	Br	214, 222, 276sh, 362	4·4, 4·4, 3·54, 4·0
(42) [b] ‡	Br	256sh, 278sh, 380, 394sh	3·96, 3·59, 4·01, 3·98
(42) [b] §	Br	356	4·11
(44)	ClO_4	201, 257, 264sh, 302, 373	4·6, 4·14, 4·12, 3·82, 3·85
(45)	Br	202, 232sh, 261, 375	4·62, 4·28, 4·22, 4·02
(46)	ClO_4	201, 231sh, 260, 373	4·63, 4·29, 4·27, 4·08
(47)	ClO_4	202, 255, 362	4·51, 4·22, 4·17

* In H_2O except where otherwise stated. † In EtOH. ‡ In 2N-NaOH. § In 2N-HBr.

[a] Spectrum recorded above 240 nm only. [b] Spectrum recorded above 250 nm only.

bromide (0·5 g) in acetonitrile (1·5 ml) was boiled under reflux for 5 h. The solid which separated was filtered off and dissolved in 60% perchloric acid, and the *perchlorate* was precipitated with ethanol–ether; yield 0·18 g (18%), m.p. 273—275° (from aqueous methanol).

4-*Bromo*-2-(p-*bromophenyl*)-1,2-*dihydro*-1-*oxo*-3-*phenylpyrido*[1,2-a]*pyrazinium Bromide* (45).—This was prepared (70% yield based on available bromine) from the bromide (13) by the procedure for the preparation of compound (44). The *bromide* yielded (from methanol–di-isopropyl ether) an amorphous yellow solid which decomposed without melting below 330° (Found: C, 45·05; H, 2·4; N, 5·1. $C_{20}H_{13}Br_3N_2O$ requires C, 44·7; H, 2·4; N, 5·2%). The *perchlorate* gave yellow plates, m.p. 181—184° (from methanol–di-isopropyl ether) (Found: N, 5·1. $C_{20}H_{13}Br_2ClN_2O_5$ requires N, 5·0%).

4-*Bromo*-3-p-*bromophenyl*-1,2-*dihydro*-1-*oxo*-2-*phenylpyrido*[1,2-a]*pyrazinium Bromide* (46).—This was prepared (78% yield based on available bromine) from the bromide (14) by the procedure for the preparation of compound (44). The *bromide* gave (from methanol–di-isopropyl ether) yellow plates which decomposed without melting below 330° (Found: N, 5·6. $C_{20}H_{13}Br_3N_2O$ requires N, 5·2%). The *perchlorate* yielded yellow-green needles, m.p. 290—292° (from aqueous methanol) (Found: C, 43·4; H, 2·3; N, 4·9. $C_{20}H_{13}Br_2ClN_2O_5$ requires C, 43·15; H, 2·35; N, 5·0%).

1-*Oxo*-2,3-*diphenyloctahydropyrido*[1,2-a]*pyrazine* (48).—A solution of the bromide (44) (0·47 g) in methanol (60 ml) was hydrogenated to completion (4 h) over Adams catalyst at room temperature and 2 atm. pressure. Catalyst and solvent were removed and the residual gum was triturated with ethanol–ether until it solidified. The *lactam hydrobromide* gave plates, m.p. 251—254° (decomp.) (from methanol–ether) (0·28 g, 70%) (Found: C, 61·6; H, 5·9; N, 7·4. $C_{20}H_{22}N_2O,HBr$ requires C, 62·0; H, 6·0; N, 7·2%). The *free base*, purified by sublimation at 165° and 0·1 mmHg, had m.p. 173—176° (Found: C, 78·15; H, 7·5; N, 9·35. $C_{20}H_{22}N_2O$ requires C, 78·4; H, 7·2; N, 9·1%). The same base was obtained in 60% yield by similarly hydrogenating the perchlorate (47).

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